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CLAIMS

What is claimed is:

1. A hydrobromide salt of 3-(4-bromo-2,6-difluoro-benzyloxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide.
2. The salt according to claim 1, wherein said salt has a X-ray powder diffraction spectrum substantially the same as the X-ray powder diffraction spectrum shown in FIG. 2.
3. The salt according to claim 2, which provides high-intensity diffraction peaks at diffraction angles (2 θ) of 8.687, 12.264, 17.374, 23.711, 24.335, and 25.769 in the X-ray powder diffraction analysis.
4. A hydrobromide salt of 3-(4-bromo-2,6-difluoro-benzyloxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide that exhibits an X-ray powder diffraction spectrum having characteristic peaks expressed in degrees (2 θ) at approximately:

2 θ	RI(%)	2 θ	RI(%)	2 θ	RI(%)	2 θ	RI(%)	2 θ	RI(%)
3.156	2.5	17.374	42.3	23.188	5.6	28.528	6.1	33.256	3.7
4.615	2.4	17.767	5.6	23.711	24.0	28.916	9.4	33.897	7.9
6.331	9.3	18.185	3.2	24.335	20.7	29.418	7.7	34.628	2.8
8.687	100.0	18.913	16.6	25.435	9.1	30.266	4.6	34.999	3.3
12.264	35.9	19.528	9.5	25.769	34.3	31.561	3.9	35.432	6.1
12.890	2.2	20.286	2.5	26.940	4.1	32.082	3.4	36.006	4.3
13.445	1.4	20.581	2.9	27.345	7.0	32.638	5.3	37.361	3.4
14.140	3.4	21.874	13.6	28.160	5.7	32.925	4.4	38.224	4.8
16.083	4.0								

5. A hemi-citrate salt of 3-(4-bromo-2,6-difluoro-benzyloxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide.
6. The salt according to claim 5, wherein said salt has a X-ray powder diffraction spectrum substantially the same as the X-ray powder diffraction spectrum shown in FIG 3.

5 7. The salt according to claim 6, which provides high-intensity diffraction peaks at diffraction angles (2θ) of 4.306, 16.317, 20.988, 21.476, 22.643, 23.384, 24.891, 27.573, and 27.840 in the X-ray powder diffraction analysis.

10 8. A hemi-citrate salt of 3-(4-bromo-2,6-difluoro-benzyloxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide that exhibits an X-ray powder diffraction spectrum having characteristic peaks expressed in degrees (2θ) at approximately:

2θ	RI(%)	2θ	RI(%)	2θ	RI(%)	2θ	RI(%)	2θ	RI(%)
3.201	14.3	13.766	12.4	18.693	15.8	24.217	28.8	29.630	17.4
4.306	79.9	14.086	7.0	19.344	23.4	24.891	76.0	31.251	14.6
6.429	7.0	14.710	9.5	20.394	16.4	25.320	20.4	31.848	14.2
8.620	6.0	15.297	16.0	20.988	32.7	25.948	28.0	32.235	11.8
9.589	5.6	16.317	100.0	21.476	30.9	26.370	25.7	34.147	11.0
10.583	6.8	17.309	14.4	21.994	27.3	27.573	47.9	35.878	16.2
11.449	20.9	17.572	16.5	22.643	48.7	27.840	32.3	37.337	12.3
12.300	8.7	18.258	13.7	23.384	76.9	28.609	19.6		

15 9. An acetate salt of 3-(4-bromo-2,6-difluoro-benzyloxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide.

20 10. The salt according to claim 9, wherein said salt has a X-ray powder diffraction spectrum substantially the same as the X-ray powder diffraction spectrum shown in FIG. 4.

25 11. The salt according to claim 10, which provides high-intensity diffraction peaks at diffraction angles (2θ) of 6.096, 12.183, 17.451, 18.288, 22.441, 23.086, and 24.439 in the X-ray powder diffraction analysis.

 12. A acetate salt of 3-(4-bromo-2,6-difluoro-benzyloxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide that exhibits an X-ray powder diffraction spectrum having characteristic peaks expressed in degrees (2θ) at approximately:

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2θ	RI(%)	2θ	RI(%)	2θ	RI(%)	2θ	RI(%)	2θ	RI(%)
6.096	21.7	16.793	4.5	21.346	8.9	27.930	5.8	32.271	4.1
8.625	2.8	17.121	12.8	22.441	57.7	28.820	10.0	33.127	5.1
11.840	2.9	17.451	33.3	23.086	19.9	29.648	6.1	35.030	3.4
12.183	21.4	17.920	8.7	24.038	7.5	30.634	3.3	36.445	3.2
14.836	4.2	18.288	100.0	24.439	20.7	31.112	3.2	37.830	3.0
15.264	9.2	20.088	3.6	24.760	11.3	31.951	2.9	39.478	2.5
15.824	5.0	20.458	11.3	25.861	5.0				

13. A p-tosylate salt of 3-(4-bromo-2,6-difluoro-benzyloxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide.

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14. The salt according to claim 13, wherein said salt has a X-ray powder diffraction spectrum substantially the same as the X-ray powder diffraction spectrum shown in FIG. 5.

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15. The salt according to claim 14, which provides high-intensity diffraction peaks at diffraction angles (2θ) of 20.446, 20.760, 22.092, 22.371, 23.190, and 26.239 in the X-ray powder diffraction analysis.

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16. A p-tosylate salt of 3-(4-bromo-2,6-difluoro-benzyloxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide that exhibits an X-ray powder diffraction spectrum having characteristic peaks expressed in degrees (2θ) at approximately:

2θ	RI(%)	2θ	RI(%)	2θ	RI(%)	2θ	RI(%)	2θ	RI(%)
6.817	50.3	13.373	53.9	18.174	21.3	23.190	65.2	28.167	34.5
7.515	28.0	14.337	18.3	18.976	40.4	24.110	30.5	29.672	19.6
7.822	22.3	15.001	22.2	19.739	36.7	25.471	40.2	31.038	19.3
11.157	15.0	15.601	21.4	20.446	100.0	25.932	50.4	31.586	21.2
12.205	24.5	16.297	14.0	20.760	74.0	26.239	61.5	35.357	19.6
12.800	30.0	16.943	32.0	22.092	81.7	27.355	48.8	36.800	16.4
13.047	43.6	17.362	23.5	22.371	70.8	27.833	39.0		

17. A L-tartrate salt of 3-(4-bromo-2,6-difluoro-benzyloxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide.

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18. The salt according to claim 17, wherein said salt has a X-ray powder diffraction spectrum substantially the same as the X-ray powder diffraction spectrum shown in FIG. 6.

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19. The salt according to claim 18, which provides high-intensity diffraction peaks at diffraction angles (2θ) of 4.061, 20.821, 21.634, 22.179, and 25.858 in the X-ray powder diffraction analysis.

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20. A L-tartrate salt of 3-(4-bromo-2,6-difluoro-benzyloxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide that exhibits an X-ray powder diffraction spectrum having characteristic peaks expressed in degrees (2θ) at approximately:

2θ	RI(%)	2θ	RI(%)	2θ	RI(%)	2θ	RI(%)	2θ	RI(%)
4.061	82.9	14.631	27.2	20.010	53.0	24.788	53.8	32.465	36.1
6.678	11.8	15.428	22.7	20.334	58.7	25.081	60.9	33.442	33.7
8.057	29.4	16.143	31.2	20.821	85.6	25.858	95.1	34.090	34.6
9.383	8.7	16.853	65.3	21.634	100.0	26.803	59.6	34.642	26.8
10.647	8.3	17.338	56.2	22.179	94.0	28.386	34.3	35.635	33.7
11.711	60.2	18.400	97.0	22.730	73.8	29.067	34.1	36.073	28.5
12.075	27.4	18.639	98.2	23.477	77.1	29.844	30.5	36.771	24.5
12.868	33.8	18.994	52.4	24.257	67.8	31.309	39.4	38.080	22.6
13.320	22.7	19.722	42.9						

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21. A hemi-succinate salt of 3-(4-bromo-2,6-difluoro-benzyloxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide which is Form A.

22. The salt according to claim 21, wherein said salt has a X-ray powder diffraction spectrum substantially the same as the X-ray powder diffraction spectrum shown in FIG. 7.

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23. The salt according to claim 22, which provides high-intensity diffraction peaks at diffraction angles (2θ) of 4.634, 16.735, 22.179, and 25.002 in the X-ray powder diffraction analysis.

24. A hemi-succinate form A salt of 3-(4-bromo-2,6-difluoro-benzyloxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide that exhibits an X-ray

- 5 powder diffraction spectrum having characteristic peaks expressed in degrees (2 θ) at approximately:

2 θ	RI(%)	2 θ	RI(%)	2 θ	RI(%)	2 θ	RI(%)	2 θ	RI(%)
4.634	100.0	13.683	13.8	17.760	20.6	22.866	38.7	27.609	23.7
6.149	15.5	14.440	13.5	18.679	18.4	23.255	39.5	30.106	14.3
9.843	6.2	14.896	21.9	19.421	30.2	24.079	44.6	30.797	13.7
11.392	11.3	15.996	14.4	20.586	29.2	25.002	70.3	37.769	11.4
11.937	19.2	16.735	67.2	22.179	60.8	26.549	26.8		

25. A hemi-succinate salt of 3-(4-bromo-2,6-difluoro-benzyloxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide which is Form B.

26. The salt according to claim 25, wherein said salt has a X-ray powder diffraction spectrum substantially the same as the X-ray powder diffraction spectrum shown in FIG. 8.

27. The salt according to claim 26, which provides high-intensity diffraction peaks at diffraction angles (2 θ) of 6.714, 15.272, 19.197, 19.457, 24.487, and 24.802 in the X-ray powder diffraction analysis.

28. A hemi-succinate form B salt of 3-(4-bromo-2,6-difluoro-benzyloxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide that exhibits an X-ray powder diffraction spectrum having characteristic peaks expressed in degrees (2 θ) at approximately:

2 θ	RI(%)	2 θ	RI(%)	2 θ	RI(%)	2 θ	RI(%)	2 θ	RI(%)
6.714	31.0	15.272	100.0	19.197	59.3	24.487	99.0	29.732	14.1
8.666	7.3	15.813	19.8	19.457	50.0	24.802	79.1	30.796	17.5
11.092	8.6	16.551	17.5	20.597	17.2	25.640	15.9	33.484	9.4
11.696	21.9	16.875	26.4	21.160	28.8	26.641	20.1	34.594	11.4
12.008	15.9	17.365	12.6	21.648	21.7	27.090	15.1	37.212	15.5
12.630	7.3	17.986	8.6	22.988	15.0	27.843	21.5	37.905	8.9
13.466	17.2	18.710	26.4	23.568	18.6	28.552	19.7	39.023	8.9
13.774	13.9								

5 29. A method of treating a hyperproliferative disorder in a mammal which comprises administering to the mammal a therapeutically effective amount of a compound according to claim 1.

10 30. The method of claim 29 wherein the method is for the treatment of a cancer selected from brain, squamous cell, bladder, gastric, pancreatic, breast, head, neck, oesophageal, prostate, colorectal, lung, renal, kidney, ovarian, gynecological and thyroid cancer.

15 31. A method for the treatment of a hyperproliferative disorder in a mammal which comprises administering to the mammal a therapeutically effective amount of a polymorph according to claim 1 in combination with an anti-tumor agent selected from the group consisting of mitotic inhibitors, alkylating agents, anti-metabolites, intercalating antibiotics, growth factor inhibitors, cell cycle inhibitors, enzymes, topoisomerase inhibitors, biological response modifiers, anti-hormones, and anti-androgens.

20 32. A pharmaceutical composition comprising an amount of a compound according to claim 1 effective to treat a hyperproliferative disorder in a mammal, and a pharmaceutically acceptable carrier.

25 33. The pharmaceutical composition of claim 32 wherein the hyperproliferative disorder is a cancer selected from brain, lung, squamous cell, bladder, gastric, pancreatic, breast, head, neck, renal, kidney, ovarian, prostate, colorectal, oesophageal, gynecological and thyroid cancer.

30 34. The pharmaceutical composition of claim 33, wherein the composition is adapted for oral administration.

35 35. The pharmaceutical composition of claim 34, wherein the pharmaceutical composition is in tablet form.

 36. A method of preventing pregnancy, comprising administering to a female mammal a compound according to claim 1.

40 37. The method of claim 36, further comprising a pharmaceutically acceptable carrier.